AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION:

Please amend page 4, the second paragraph beginning at line 11, as follows:

Preferably, in the modified glucose dehydrogenase of the invention, ~~Gln192~~ glutamine at position 168 or ~~Leu193~~ leucine at position 169 of the amino acid sequence defined in SEQ ID NO: 1 of water-soluble PQQGDH derived from *Acinetobacter calcoaceticus* or an amino acid residue in an equivalent position from other species are replaced with another amino acid residues.

Please amend page 4, the third paragraph beginning at line 16, as follows:

In another aspect, the invention features a modified glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme wherein ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with another amino acid residue. Preferably, ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine, glycine, glutamic acid, leucine, phenylalanine, serine or aspartic acid.

Please amend page 4, the fourth paragraph beginning at line 23, as follows:

In another aspect, the invention features a modified glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme wherein both ~~Gln192~~ glutamine at position 168 and ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 are replaced with other amino acid residues. Preferably, ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine, glycine, glutamic acid,

leucine, phenylalanine, serine or aspartic acid. More preferably, ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with glutamic acid, and ~~Gln192~~ glutamine at position 168 is replaced with alanine, glycine, glutamic acid, leucine, phenylalanine, serine or aspartic acid.

Please amend page 5, first paragraph, beginning at line 1, as follows:

In another aspect, the invention features a modified glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme wherein ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with another amino acid residue, and ~~Asn452~~ asparagine at position 428 is replaced with another amino acid residue. Preferably, ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with glutamic acid. More preferably, ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with glutamic acid, and ~~Asn452~~ asparagine at position 428 is replaced with threonine.

Please amend page 5, second paragraph, beginning at line 11, as follows:

In another aspect, the invention features a modified glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme wherein ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with another amino acid residue, and ~~Asn452~~ asparagine at position 428 is replaced with another amino acid residue. Preferably, ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine, glycine, glutamic acid, leucine, phenylalanine, serine or aspartic acid, and ~~Asn452~~

asparagine at position 428 is replaced with another amino acid residue. More preferably, ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine, glycine, glutamic acid, leucine, phenylalanine, serine or aspartic acid, and ~~Asn452~~ asparagine at position 428 is replaced with threonine.

Please amend page 5, third paragraph, line 24, as follows:

In another aspect, the invention features a modified glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme wherein ~~Leu193~~ leucine at position 169 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with another amino acid residue. Preferably, ~~Leu193~~ leucine at position 169 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine, glycine, methionine, tryptophan or lysine.

Please amend page 7, first paragraph, beginning at line 1, as follows:

other species are replaced with other amino acid residues. Preferably, ~~Gln192~~ glutamine at position 168 of the amino acid sequence defined in SEQ ID NO: 1 is replaced with alanine or glycine, and/or ~~Leu193~~ leucine at position 169 is replaced with alanine, glycine, methionine, tryptophan or lysine.

Please amend page 7, second paragraph, beginning at line 6, as follows:

In another aspect of the modified PQQGDH of the invention, in addition to the modifications as described above, ~~Asp167~~ aspartate at position 143 of the amino acid sequence defined in SEQ ID NO: 1 is also replaced with another amino acid, preferably with glutamic acid. Also preferably,

in the modified PQQGDH of the present invention, in addition to the modifications as described above, ~~Asn452~~ asparagine at position 428 of the amino acid sequence defined in SEQ ID NO: 1 is also replaced with another amino acid, preferably with threonine. Involvement of ~~Asp167~~ aspartate at position 143 and ~~Asn452~~ asparagine at position 428 of the amino acid sequence defined in SEQ ID NO: 1 in recognition and binding of substrate by PQQGDH is described in Japanese Patent Public Disclosure Nos. 2001-346587 and 2001-197888, respectively. In general, however, no prediction can be made regarding the changes of substrate selectivity and enzyme activity which may be caused by simultaneously altering the amino acid residues in different domains. In some cases the enzyme activity will be completely abolished. Therefore, it was a surprising discovery in the present invention that improved selectivity for glucose can be achieved by introducing double mutations.

Please amend page 12, Example 1, as follows:

Example 1

Construction of gene encoding modified PQQGDH enzyme

Mutagenesis was carried out based on the structural gene of PQQGDH derived from *Acinetobacter calcoaceticus* (SEQ ID NO:2). pGB2 plasmid was constructed by inserting the structural gene of PQQGDH derived from *Acinetobacter calcoaceticus* into the multi-cloning site of pTrc99A vector (Pharmacia) (Fig.1). The nucleotide sequence encoding ~~Gln192~~ glutamine at position 168 or ~~Leu193~~ leucine at position 169 of the amino acid sequence defined in SEQ ID NO: 1 was replaced with the nucleotide sequence encoding alanine, glycine, methionine, tryptophan or lysine by standard method of site-directed mutagenesis. Also the nucleotide sequence encoding ~~Asp167~~ aspartate at position 143 and ~~Asn452~~ asparagine at

position 428 of the amino acid sequence defined in SEQ ID NO: 1 was replaced with the nucleotide sequence encoding glutamic acid and glycine, respectively. Site specific mutagenesis was performed using the pGB2 plasmid as shown in Fig.2. The sequences of synthetic oligonucleotide target primers used for mutagenesis are shown in Table 1. In order to construct a mutant containing two mutations, two oligonucleotide target primers were used simultaneously for mutagenesis.